What is claimed is:

1. A chimeric nuclease comprising: (i) a DNA binding domain; (ii) a cleavage domain; and (iii) a nuclear localization signal.

2. The chimeric nuclease of claim 1, wherein the DNA binding domain binds to a recognition sequence comprising at least 6 designated nucleotides.

3. The chimeric nuclease of claim 1, wherein the DNA binding domain comprises at least one zinc finger domain.

4. The chimeric nuclease of claim 1, wherein the DNA binding domain comprises three or more zinc finger domains.

5. The chimeric nuclease of claim 1, wherein the cleavage domain comprises a cleavage domain of a type IIs restriction endonuclease.

6. The chimeric nuclease of claim 1, wherein the cleavage domain comprises a cleavage domain of a FokI restriction endonuclease.

7. The chimeric nuclease of claim 1, wherein the DNA binding domain comprises three zinc finger domains and binds to a recognition sequence comprising 9 designated nucleotides, and wherein the cleavage domain is a cleavage domain of a FokI restriction endonuclease.

8. A chimeric nuclease comprising:
(a) a cleavage domain; and
(b) a DNA binding domain comprising at least three zinc fingers,
wherein the DNA binding domain binds to a recognition sequence that occurs at a position in a mammalian genome within at least 500 base pairs of an allele that contributes to a genetic disorder, and wherein the recognition sequence comprises at least 9 nucleotides.

9. A complex comprising a first chimeric nuclease and a second chimeric nuclease, wherein the first chimeric nuclease comprises a cleavage domain and a DNA binding domain, and wherein the second chimeric nuclease comprises a cleavage domain and a DNA binding domain.

10. The complex of claim 9, wherein the first chimeric nuclease comprises a DNA binding domain that comprises at least three zinc finger domains and that recognizes a sequence comprising at least 9 designated nucleotides.

11. The complex of claim 10, wherein the second chimeric nuclease comprises a DNA binding domain that comprises at least three zinc finger domains and that recognizes a sequence comprising at least 9 designated nucleotides.

12. The complex of claim 9, wherein the first chimeric nuclease and/or the second chimeric nuclease further comprises a nuclear localization signal.

13. A nucleic acid encoding a chimeric nuclease, wherein the chimeric nuclease comprises: (i) a DNA binding domain; (ii) a cleavage domain; and (iii) a nuclear localization signal (NLS).

14. A vector comprising the nucleic acid of claim 13.

15. The vector of claim 14, wherein the nucleic acid encoding the chimeric nuclease is operably linked to a promoter for expression in a mammalian cell.

16. The vector of claim 15, wherein the promoter is an inducible promoter.

17. The vector of claim 14, wherein the vector is a viral vector.

18. A nucleic acid encoding a chimeric nuclease, the chimeric nuclease comprising:
(a) a cleavage domain; and
(b) a DNA binding domain comprising at least three zinc fingers,

wherein the DNA binding domain binds to a recognition sequence that occurs at a position in a mammalian genome within at least 500 base pairs of an allele that contributes to a genetic disorder, and wherein the recognition sequence comprises at least 9 nucleotides.

19. A vector comprising the nucleic acid of claim 18.

20. A vector comprising
(a) a nucleic acid encoding a first chimeric nuclease; and
(b) a nucleic acid encoding a second chimeric nuclease,
wherein the second chimeric nuclease forms a heterodimer with said first chimeric nuclease.

21. A vector comprising:
(1) a nucleic acid encoding a chimeric nuclease that comprises: (i) a DNA binding domain; and (ii) a cleavage domain; and
(2) a nucleic acid comprising a repair substrate that comprises: (i) a nucleic acid sequence that is substantially identical to a region flanking a target sequence in chromosomal DNA; and (ii) a nucleic acid sequence which replaces the target sequence upon recombination between the repair substrate and the target sequence.

22. The vector of claim 21, wherein the chimeric nuclease further comprises a nuclear localization signal.

23. The vector of claim 21, wherein the nucleic acid encoding the chimeric nuclease is operably linked to a promoter.

24. The vector of claim 23, wherein the promoter is an inducible promoter.

25. The vector of claim 23, wherein the vector is a viral vector.

26. The vector of claim 21, further comprising a nucleic acid encoding a second chimeric nuclease, wherein the second chimeric nuclease forms a heterodimer with said chimeric nuclease.

27. A cell comprising a vector of claim 14.

28. A mammalian cell comprising: (a) a chimeric nuclease; and (b) a repair substrate, wherein the chimeric nuclease comprises:
(i) a DNA binding domain; and
(ii) a cleavage domain,
and wherein the repair substrate comprises:
(i) a nucleic acid sequence that is substantially identical to a region flanking a target sequence in chromosomal DNA; and
(ii) a nucleic acid sequence which replaces the target sequence upon recombination between the repair substrate and the target sequence.

29. The cell of claim 28, wherein the cell comprises a vector, the vector comprising:
(a) a nucleic acid encoding the chimeric nuclease, and
(b) a nucleic acid encoding the repair substrate.

30. The cell of claim 28, wherein the repair substrate is operably linked to a promoter in a vector.

31. The cell of claim 28, wherein the chimeric nuclease is encoded by a nucleic acid that is operably linked to a promoter in a vector.

32. The cell of claim 30, wherein the promoter is an inducible promoter.

33. The cell of claim 31, wherein the promoter is an inducible promoter.

34. The cell of claim 28, wherein the chimeric nuclease further comprises a nuclear localization signal.

35. The cell of claim 28, wherein the DNA binding domain of the chimeric nuclease comprises a zinc finger domain.

36. The cell of claim 28, wherein the cleavage domain comprises a cleavage domain of a type IIs restriction endonuclease.

37. The cell of claim 36, wherein the cleavage domain comprises a FokI cleavage domain.

38. The cell of claim 28, wherein the mammalian cell is a human cell.

39. The cell of claim 28, wherein the cell is an in vitro cell.

40. A mammalian cell comprising a nucleic acid encoding a chimeric nuclease and a nucleic acid comprising a repair substrate, wherein the chimeric nuclease comprises:
(i) a DNA binding domain; and
(ii) a cleavage domain,
and wherein the repair substrate comprises:
(i) a nucleic acid sequence that is substantially identical to a region flanking a target sequence in chromosomal DNA; and
(ii) a nucleic acid sequence which replaces the target sequence upon recombination between the repair substrate and the target sequence.

41. A recombinant transfection system, comprising: (i) the vector of claim 14; and (ii) a gene delivery composition for delivering said vector to a cell and causing said cell to be transfected with said vector.

42. The recombinant transfection system of claim 41, wherein said gene delivery composition is selected from the group consisting of a recombinant viral particle, a liposome, and a poly-cationic nucleic acid binding agent.

43. A method of changing a target sequence in genomic DNA of a mammalian cell, comprising:

(a) introducing a chimeric nuclease, or nucleic acid encoding the chimeric nucleic acid, into the cell, wherein said chimeric nuclease comprises: (i) a DNA binding domain; and (ii) a cleavage domain; and

(b) introducing a repair substrate into the cell, wherein said repair substrate comprises: (i) a nucleic acid sequence that is substantially identical to a region surrounding the target sequence; and (ii) a nucleic acid sequence which changes the target sequence upon recombination between the repair substrate and the target sequence,

whereby the target sequence is changed by the repair substrate upon recombination.

44. The method of claim 43, wherein the target sequence contains an allele that contributes to a disease that is repaired by the repair substrate.

45. The method of claim 43, wherein the target sequence is modified by the repair substrate.

46. The method of claim 43, wherein the target sequence is situated in a gene that is attenuated or inactivated by the repair substrate.

47. The method of claim 43, wherein the target sequence is replaced by a heterologous sequence in the repair substrate.

48. The method of claim 47, wherein the heterologous sequence comprises the coding sequence of a transgene.

49. The method of claim 47, wherein the target sequence is selected such that the coding sequence of a transgene is inserted at a transcriptionally active site.

50. The method of claim 43, wherein the repair substrate is operably linked to a promoter in a vector.

51. The method of claim 43, wherein introducing the chimeric nuclease into the cell comprises introducing a nucleic acid encoding the chimeric nuclease into the cell, whereby the chimeric nuclease is produced in cell.

52. The method of claim 51, wherein the nucleic acid encoding the chimeric nuclease and the repair substrate are present in a single vector introduced into the cell.

53. The method of claim 51, wherein the nucleic acid encoding the chimeric nuclease is operably linked to a promoter in a vector.

54. The method of claim 53, wherein the promoter is an inducible promoter.

55. The method of claim 43, wherein the chimeric nuclease protein is introduced into the cell as a protein.

56. The method of claim 43, wherein the chimeric nuclease further comprises a nuclear localization signal.

57. The method of claim 43, wherein the DNA binding domain of the chimeric nuclease comprises a zinc finger binding domain.

58. The method of claim 43, wherein the cleavage domain comprises a cleavage domain of a restriction endonuclease.

59. The method of claim 58, wherein the cleavage domain comprises a FokI cleavage domain.

60. The method of claim 43, wherein the chimeric nuclease forms a homodimer of two identical chimeric nucleases.

61. The method of claim 43, wherein the chimeric nuclease forms a heterodimer of two different chimeric nucleases.

62. The method of claim 43, wherein the target sequence includes an allele that participates in the causation of a disease to be corrected by gene targeting.

63. The method of claim 43, wherein the mammalian cell is an in vitro human cell.

64. The method of claim 43, wherein the cell is an in vitro cell.

65. A method for ameliorating, treating or preventing, in an individual in need thereof, a disease caused, in part or in whole, by a genomic target sequence, the method comprising:
(a) introducing a chimeric nuclease into a cell, wherein said chimeric nuclease comprises: (i) a DNA binding domain; and (ii) a cleavage domain; and
(b) introducing a repair substrate into the cell, wherein said repair substrate comprises: (i) a nucleic acid sequence that is substantially identical to a region flanking the target sequence in chromosomal DNA; and (ii) a nucleic acid sequence which replaces the target sequence upon recombination between the repair substrate and the target sequence,
whereby the target sequence is altered in the cell, and the disease is ameliorated, treated or prevented.

66. The method of claim 65, wherein the cell is an in vitro cell obtained from the individual, and wherein the cell, or progeny thereof, is reintroduced to the individual after the target sequence is altered.

67. The method of claim 65, wherein the cell is a stem cell or a population of cells comprising the stem cell.

68. The method of claim 65, wherein the cell is an in vitro cell obtained from a donor.

69. The method of claim 68, wherein the cell is reintroduced to the individual after the target sequence is altered.

70. The method of claim 68, wherein the cell is a stem cell or a population of cells comprising the stem cell.

71. The method of claim 65, wherein the cell is an in vivo cell in the individual.

72. The method of claim 71, wherein introducing the chimeric nuclease to the cell comprising transfecting the cell with a nucleic acid encoding the chimeric nuclease, whereby the chimeric nuclease is produced in the cell.

73. The method of claim 72, wherein the nucleic acid encoding the chimeric nuclease and the repair substrate are present in a single vector introduced into the cell.

74. The method of claim 65, wherein the repair substrate is operably linked to a promoter in a vector.

75. The method of claim 65, wherein introducing the chimeric nuclease into the cell comprises introducing a nucleic acid encoding the chimeric nuclease into the cell, whereby the chimeric nuclease is produced in cell.

76. The method of claim 65, wherein the nucleic acid encoding the chimeric nuclease is operably linked to a promoter in a vector.

77. The method of claim 76, wherein the promoter is an inducible promoter.

78. The method of claim 65, wherein the chimeric nuclease is directly introduced as a protein into the cells of the individual.

79. The method of claim 65, wherein the chimeric nuclease further comprises a nuclear localization signal.

80. The method of claim 65, wherein the DNA binding domain of the chimeric nuclease comprises a zinc finger domain.

81. The method of claim 65, wherein the cleavage domain comprises a cleavage domain of a type IIs restriction endonuclease.

82. The method of claim 81, wherein the cleavage domain comprises a FokI cleavage domain.

83. The method of claim 65, wherein the chimeric nuclease forms a homodimer of two identical chimeric nucleases.

84. The method of claim 65, wherein the chimeric nuclease forms a heterodimer of two different chimeric nucleases.

85. The method of claim 65, wherein the individual is a human.

86. The method of claim 65, wherein the disease is selected from the group consisting of severe combined immunodeficiency (SCID), sickle cell disease, and hemophilia.

87. The method of claim 65, wherein the disease is an infectious disease, and wherein the genomic target sequence contributes to the susceptibility of the individual to the infectious disease.

88. The method of claim 87, wherein the infectious disease is an HIV infection, and wherein the genomic target sequence is at least a portion of a gene for a cell surface protein that participates in cell entry by HIV, and wherein altering the target sequence inhibits cell entry by HIV.

89. The method of claim 88, wherein the cell is a T cell or a T cell progenitor.

90. A method of designing a nucleic acid encoding a chimeric nuclease, comprising:
(a) selecting a mammalian target sequence for gene targeting;
(b) identifying a possible DNA binding sequence within workable proximity of the target sequence;

(c) designing a nucleic acid encoding a DNA binding domain that binds to the DNA binding sequence identified in (b); and
(d) coupling the nucleic acid encoding the DNA binding domain in (c) to a nucleic acid encoding a cleavage domain to make a nucleic acid comprising the coding sequence for the chimeric nuclease.

91. The method of claim 90, further comprising coupling a nucleic acid encoding a nuclear localization signal to the nucleic acid comprising the coding sequence for the chimeric nuclease.

92. The method of claim 90, wherein the DNA binding domain comprises a zinc finger binding domain.

93. The method of claim 90, wherein the cleavage domain comprises a cleavage domain of a type IIs restriction endonuclease.

94. The method of claim 93, wherein the cleavage domain comprises a FokI cleavage domain.

95. The method of claim 90, further comprising:
(e) selecting a second possible DNA binding sequence within workable proximity of the target sequence and positioned such that a chimeric nuclease bound to the second possible DNA binding sequence acts conjointly with a chimeric nuclease bound to the possible DNA binding sequence of (b); and
(f) generating a nucleic acid encoding a chimeric nuclease that binds to the second possible DNA binding sequence and acts conjointly with the chimeric nuclease encoded by the nucleic acid of (d).

96. The method of claim 90, further comprising testing the chimeric enzyme for toxicity in a cell.

97. The method of claim 90, further comprising testing the cleavage site specificity of the chimeric enzyme.